REMARKS/ARGUMENTS

Status of the Claims

Upon entry of the present amendment, claims 4-8 are pending. Claims 1-3 and 9-14 are canceled without disclaimer or prejudice to renewal. Claims 4-6 are amended to set forth that the growth medium comprises (i) hepatocyte growth factor (HGF) and fibroblast growth factor-2 (FGF-2), (ii) HGF and epidermal growth factor (EGF), or (iii) HGF, FGF-2 and EGF. Support is found, for example, in claims 1-3 as originally filed; on page 7, lines 4-9; page 9, lines 15-24; page 10, lines 9-18; page 10, line 22 through page 11, lines 10; page 13, lines 23-25; page 14, lines 5-7; page 18, lines 8-20; page 19, lines 10-14; page 29, line 23 to page 30, line 1; page 30, lines 6-16; page 33, line 24 through page 35, line 11 (particularly Table 1); page 36, line 10 through page 38; page 38, lines 9-13; and Figures 1, 3 and 5.

No new matter has been added by the present amendments, and the Examiner is respectfully requested to enter them.

Claim Objections

The Examiner has objected to claims 4-6 for depending from claim 1. In response, Applicants have amended claims 4-6 to be in independent form.

Rejection under 35 U.S.C. § 102(e)

The Examiner has rejected claims 4-6 and 8 under 35 U.S.C. § 102(e) as allegedly anticipated by U.S. Patent No. 6,589,728 ("Csete"). To the extent that this rejection applies to the amended claims, this rejection is respectfully traversed.

For a reference to anticipate a claim, it must teach or suggest, either expressly or inherently, each limitation of the claim. *See*, M.P.E.P. § 2131.

Here, Csete discloses a long list of potential growth factors for use in culturing neural progenitor cells *in vitro*. The crux of the invention in Csete is controlling oxygen levels and using subatmospheric oxygen levels in culture to isolate, maintain or enrich stem or progenitor cells. *See*, abstract of Csete. Csete do not describe using any single growth factor

among the long list of growth factors for culturing, proliferating or differentiating neural stem cells. Csete, at column 7, lines 46-58. To the contrary, Csete disclose that to induce differentiation to neurons and glia, fibroblast growth factor beta (FGFb) is removed from the media. Csete at column 15, lines 63-65. Moreover, Csete is completely silent on any combination of growth factors in the medium, much less the specific combinations of HGF and FGF-2, HGF and EGF, or HGF, FGF-2 and EGF recited in the present methods.

In view of the foregoing, Csete clearly does not anticipate the claimed methods. Accordingly, the Examiner is respectfully requested to withdraw the present rejection.

Rejection under 35 U.S.C. § 103(a)

The Examiner has rejected claim 7 under 35 U.S.C. § 103(a) as allegedly rendered obvious by Csete in view of U.S. Patent No. 5,753,505 ("Luskin"). To the extent that is rejection applies to the amended claims, this rejection is respectfully traversed.

To establish a *prima facie* case of obviousness, three basic criteria must be met: (1) there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings; (2) there must be a reasonable expectation of success; and (3) the prior art reference must teach or suggest all the claims limitations. MPEP§2143.

Here, the combined disclosures of Csete and Luskin do not disclose or suggest all of the limitations of the claims. As discussed above, Csete does not disclose or suggest including any combination of growth factors in the medium, much less the specific combinations of HGF and FGF-2, HGF and EGF, or HGF, FGF-2 and EGF recited in the present methods. Luskin does not supply the elements missing from Csete.

Furthermore, the Examiner is respectfully requested to kindly note the unexpected and superior results of the present methods as shown in Figure 1(b) and Table 1 (page 33, line 24 through page 35, line 11 and Figure 1(b)). As shown in Table 1, the proliferation of neural stem cells (neurospheres) cultured in growth medium in the presence of (i) HGF and FGF-2 or (ii) HGF and EGF was unexpectedly *more that triple the proliferation* in comparison to neural stem cells cultured in HGF alone. The proliferation of neural stem cells cultured in growth medium in

the presence of HGF and FGF-2 and EGF was unexpectedly *more that quaduple the proliferation* in comparison to neural stem cells cultured in HGF alone. Whereas neural stem cells cultured in HGF alone produced a total cell number of about 900 cells/well, neural stem cells cultured in (i) HGF and FGF-2, (ii) HGF and EGF, and (iii) HGF, FGF-2 and EGF produced a total number of about (i) 3100 cells/well, (ii) 2830 cells/well, and (iii) 3820 cells/well, respectively. The unexpected results in Table 1 are also supported by data shown in Figure 1(b).

In view of the foregoing, it is clear that the combined disclosures of Csete and Luskin do not *prima facie* render the present methods obvious. Regardless, the surprising and unexpected successes of the present methods rebut any alleged *prima facie* obviousness. Accordingly, the Examiner is respectfully requested to withdraw the present rejection.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,

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